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A STUDY OF ANTI CONVULSANT ACTIVITY OF SYZYCIUM CUMINI LEAVES IN WISTER RATS

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Abstract:
Epilepsy is a chronic CNS disorder characterized by brief episodes of seizures and excessive EEG discharge. Syzygium cumini used as a herbal medicine and is well known for its traditional uses such as expectorants, diuretics, laxative etc. The qualitative phytochemical analysis of ethanolic extract of Syzygium cumini. It contains alkaloids, Carbohydrates, Glycosides, Flavonoids, Terpenes, Tannins Proteins, Amino Acids. The Ethanol extract of Syzygium cumini delayed the onset and reduced the duration of convulsion in MES and PTZ induced convulsion models and can be used as an adjuvant therapy against cognitive deficit in convulsions. The extract also shows significant decrease in lipid peroxidation level and increase in reduced glutathione level, indicates that EESC possess good antioxidant activity. Also, EESC significantly increased the level of inhibitory neurotransmitter GABA and also showed increase in DA, NA and 5-HT levels. Hence it can be concluded that the EESC possesses good anticonvulsant activity. Further studies are needed to explore the mechanism as well as the active principle responsible for the anticonvulsant activity of Syzygium cumini.

KEY WORDS: *Anticonvulsant activity, Syzygium cumini, Leaves, Epilepsy, Ethanolic extract*

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INTRODUCTION:

Epilepsy is a common neurological disorder, affecting over 65 million people worldwide[1]. It is frequently related to cognitive and memory deficits causing significant morbidity [2-3]. In focal epilepsy, the "epileptogenic zone" was first defined as the cortical region sufficient for initiating seizures, that its removal is necessary for complete abolition of seizures [4]. Later, the definition was further reduced to the minimal resection or inactivation of cortical tissue for seizure freedom [5]. On the other hand, from other perspectives in the field it was proposed that the "epileptogenic zone" is not simply the "what-to-remove-area" [6]. In other words, it was supposed that the epileptogenic zone may not fully overlap with the cortical area needed to be resected according to anatomo-electro-clinical correlations [7]. Notably, epileptic clinical manifestations do not result solely from the activity in the seizure onset zone, but rather depend mainly on the propagation of epileptic activity to other structures, a process which in some of the cases extends to secondary generalization. Therefore, propagation of epileptic activity has a critical role in determining the severity of seizures and the resulting disability.

Syzygium cumini (S. cumini) (L.) Skeels is one of the best-known species and it is very often cultivated. The synonyms of S. cumini are Eugenia jambolana Lam., Myrtus cumini Linn., Syzygium jambolana DC., Syzygium jambolanum (Lam.) DC., Eugenia djouant Perr., Calyptranthes jambolana Willd., Eugenia cumini (Linn.) Druce. and Eugenia caryophyllifolia Lam. It is commonly known as jambolan, black plum, jamun, java plum, Indian blackberry, Portuguese plum, Malabar plum, purple plum, Jamaica and damson plum. Jambolan is a large evergreen and densely foliaceous tree with greyish-brown thick bark, exfoliating in woody scales. The wood is whitish, close grained and durable; affords brown dyes and a kind of a gum Kino. The leaves are leathery, oblong-ovate to elliptic or obovate-elliptic with 6 to 12 centimeters long (extremely variable in shape, smooth and shining with numerous nerves uniting within the margin), the tip being broad and less acuminate. Jambolan is rich in compounds containing anthocyanins, glucoside, ellagic acid, isoquercetin, kaemferol and myrecetin. The seeds are claimed to contain alkaloid, jambosine, and glycoside jambolin or antimellin, which halts the diastatic conversion of starch into sugar and seed extract has lowered blood pressure by 34.6% and this action is attributed to the ellagic acid content. The seeds have been reported to be rich in flavonoids, a well-known antioxidant, which accounts for the scavenging of free radicals and protective effect on antioxidant enzymes and also found to have high total phenolics with significant antioxidant activity and are fairly rich in protein and calcium. Java plums are rich in sugar, mineral salts, vitamins C, PP which fortifies the beneficial effects of vitamin C, anthocyanins and flavonoids [7-14].

In recent year there has been a tremendous increase in demand for herbal drugs due to its safety, efficacy and better therapeutic results and also due to its economic pricing as compared to synthetic or allopathic drugs, which have several therapeutic complications. The selection of this plant, Syzygium cumini was made on the basis of its High therapeutic value, Easy availability, Degree of research work which is not done. Very less pharmacological studies have been carried out on the leaves of Syzygium cumini. Hence, I have decided to choose Syzygium cumini on which detailed studies on Preliminary Phytochemical and Pharmacological actions such as Anti-convulsant is done.

MATERIALS AND METHODS:

Plant collection and identification

The whole plant of Syzygium cumini collected in the month of febravery, 2022 from Hyderabad. The plant materials were identified and authenticated by Prof. Madhav Shetty, Dept. of botany, Taxonomist, SV University, Tirupati. A voucher was kept in the Department of Pharmacognosy for reference

Preparation of plant extract

The freshly collected whole plant of this plant was shopped and dried. The dried material was powder. The powdered plant material (250 g) was extracted by hot continuous soxhlet extraction method and the plant material was extracted with Ethanol in a soxhlet apparatus.

Phytochemical Qualitative Analysis

Chemical tests performed in the screening and identification of phytochemical constituents in the tested medicinal plants were carried out in extracts as well as powder specimens using the standard procedures.

Experimental Animals

The present study was conducted after obtained approval from the Institutional Animal Ethics Committee; the protocol met the requirements of national guidelines of CPCSEA.

Animals and management

Healthy adult Wistar albino rats of either sex weighing 180-250g will be selected. The animals will

be housed in large, spacious, hygienic cages during the course of experimental period. The animal house will be well maintained and the animals will have 12 1 hour day and night schedule with a temperature [64-79°F] maintained at standard experimental condition. The animals will be fed with standard rodent pellet feed and water ad libitum. The animals will be fasted 12 hours prior to the experiment with free access to only water 42.

Acute toxicity study

Rats were kept overnight fasting prior to drug administration. A total of five animals were used which received a single oral dose (2000mg/kg) of Ethanol extract of the root of Syzygium cumini. After administration of the test extract, food was withheld further 3–4hr. Animals were observed individually at least once during the first 30min after dosing, periodically during the first 24hr (with special attention during the first 4hr) and daily thereafter for a period of 14days. Once daily, cage side observations included changes in skin and fur, eyes and mucous membrane (nasal) and also respiratory rate, circulatory (heart rate and blood pressure), autonomic (salivation, lacrimation, perspiration, piloerection, urinary incontinence, and defecation) and central nervous system (ptosis, drowsiness, gait, tremors and convulsion) changes. Mortality, if any, was determined over a period of 2 weeks. LD50 was done as per OECD guidelines for fixing the dose for biological evaluation.

Evaluation of antiepileptic activity of EESC

Maximal electroshock seizure [MES] model Experimental design

Wistar albino rats weighed around 150-250g were used for the study. Rats were divided into four groups of 5 animals each [15].

Model I: Maximal electroshock seizure [MES] Model

Group 1:Vehicle control [Equivalent normal saline i.p]

Group 2:Standard [Diphenylhydantoin 25 mg/Kg BW i.p]

Group 3:Syzygium cumini low dose (75 mg/kg) orally

Group 4:Syzygium cumini high dose (150 mg/kg) orally

Procedure

Animals in the control group [Group 1] will be administered equivalent volume of normal saline by i.p route. Animals in Group 2 will be administered standard drug Diphenylhydantoin. In Groups 3 and 4 Syzygium cumini low dose and high dose will be administered by oral route in 1% Sodium lauryl sulphate solution respectively. After 30 minutes of administration of above drugs, all the rats will be given electroshock with electro convulsiometer through ear electrodes [after moistening the ear of animals with drop of normal saline] at intensity of 150 mA, 60Hz for 0.2 seconds. There after various parameters will be recorded.

A. Pentylenetetrazol [PTZ] model Experimental design

Wistar albino rats weighed around 150-250g were used for the study. Rats were divided into four groups of 5 animals each.

Model II: Pentylenetetrazole Model

Group 1:Vehicle control [Equivalent normal saline i.p]

Group 2:Standard Sodium valproate (150 mg/Kg BW i.p)

Group 3:Syzygium cumini low dose (75 mg/kg) orally

Group 4:Syzygium cumini high dose (150 mg/kg) orally

Procedure

Animals in the control group [Group 1] will be administered equivalent volume of normal saline by i.p route. Animals in Group 2 will be administered standard drug Sodium Valproate. In Groups 3 and 4 Syzygium cumini low dose and high dose will be administered by oral route in 1% Sodium lauryl sulphate solution respectively. After 30 minutes of administration of above drugs, all the animals will be given Pentylenetetrazol [PTZ] and the various parameters will be recorded [16].

Statistical analysis

The datas of all the parameters were analyzed using the software Graph pad Prism 5. Analysis of variance (ANOVA); one way ANOVA followed by Dunnet's test was performed. The values were expressed as Mean ± SEM.

RESULTS

Phytochemical Analysis

Table No.1: Phytochemical Analysis

S. No	Phytochemicals	Inference
1	Alkaloids	+
2	Proteins and Amino acids	+
3	Tannins	+
4	Flavonoids	+
5	Terpenes	+
6	Phytosterol	-
7	Saponin	-
8	Glycosides	+
9	Phenolic compounds	+
10	Carbohydrates	+

+, Presence of the compound
-, Absent

The qualitative phytochemical analysis of ethanolic extract of Syzygium cumini. It contains alkaloids, Carbohydrates, Glycosides, Flavonoids, Tanins Proteins, Amino Acids.

Acute toxicity study

The acute toxicity test was performed by using the Ethanol extract at concentrations 2000 mg/kg, 1000 mg/kg, 900 mg/kg, 850 mg/kg, 800 mg/kg and 750 mg/kg. As it is a natural substance and is not expected to be particularly toxic. Hence 2000 mg/kg of the test animal was administered orally. And 3 animals were died. As mortality was observed after administration of 2gm/kg body weight, then a lower dose of 1000 mg/kg and 900 mg/kg was given. And mortality was observed for all animals for both doses. Hence a lower dose of 850 mg/kg was given. Two animals died and one animal survived after administration of 850 mg/kg. Hence a lower dose of 800 mg/kg was given. Two animals survived and one animal died for 800 mg/kg. Then a dose of 750 mg/kg was given. All animals survived for 750 mg/kg. and no signs of toxicity was observed following administration of 750 mg/kg. Hence *Syzygium cumini w a s* found to be safe at 750 mg/kg.

Table No 2: Acute toxicity study of *Syzygium cumini*

No. of animals used	Dose (mg/kg)	No.of animals survived
3	2000	0
3	1000	0
3	900	0
3	850	1
3	800	2
3	750	3

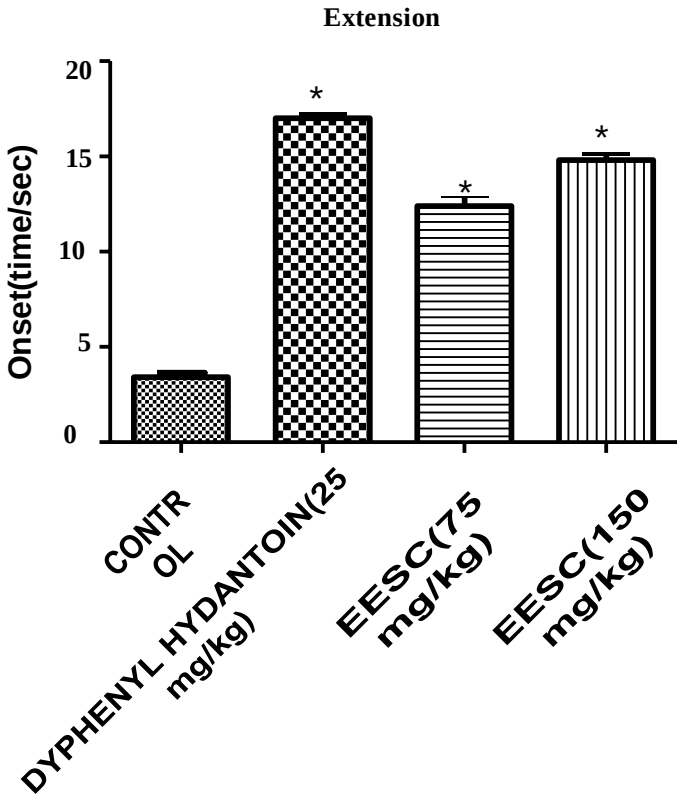
Evaluation of antiepileptic activity

Table No 3: Effect of Ethanol extract of *Syzygium cumini on* onset of hind limb extension in MES induced seizures models

Groups	Onset time (sec)		Recovery/ Mortality
	Extension	Clonus	
Control	3.40± 0.24	33.20± 1.15	Recovery
Diphenylhydantoin (25mg/kg)	17.00±0.31 *	0***	Recovery
EESC(75 mg/kg)	12.40± 0.50*	0***	Recovery
EESC(150mg/kg)	14.80± 0.37*	0***	Recovery

Statistical comparison: One way ANOVA, followed by Dunett's multiple comparison test. Standard, EESC (low dose) and EESC (High dose) are compared with control ($p<0.05$-*, $p<0.01$**, $p<0.001$***)

Figure No 1: Effect of Ethanol extract of *Syzygium cumini* on onset of hindlimb extension in MES induced seizures models



Statistical comparison: One way ANOVA, followed by Dunett's multiple comparison test. Standard, EESC (low dose) and EESC (High dose) are compared with control ($p<0.05$-*, $p<0.01$**, $p<0.001$***)

Table No 4: Effect of Ethanol extract of *Syzygium cumini on* MES induced seizures models

Groups	Flexion	Extension	Clonus	Stupor	Recovery/ Mortality
Control	5.60±0.4	18.6±0.5	24±1.68	50.40±1.77	Recovery
Diphenylhydantoin (25 mg/kg)	2.20±0.20***	4±1.04***	0***	11.00±0.44***	Recovery
EESC (75 mg/kg)	3.60±0.24***	6±0.66***	0***	19.40±0.60***	Recovery
EESC (150 mg/kg)	2.80±0.20***	5.4±1.50***	0***	14.40±0.67***	Recovery

Statistical comparison: One way ANOVA, followed by Dunett's multiple comparison test. Standard, EESC (low dose) and EESC (HIGH DOSE) are compared with control ($p<0.05$-*, $p<0.001$**, $p<0.0001$***)

Figure No 2: Effect of EESC on duration of flexion after MES

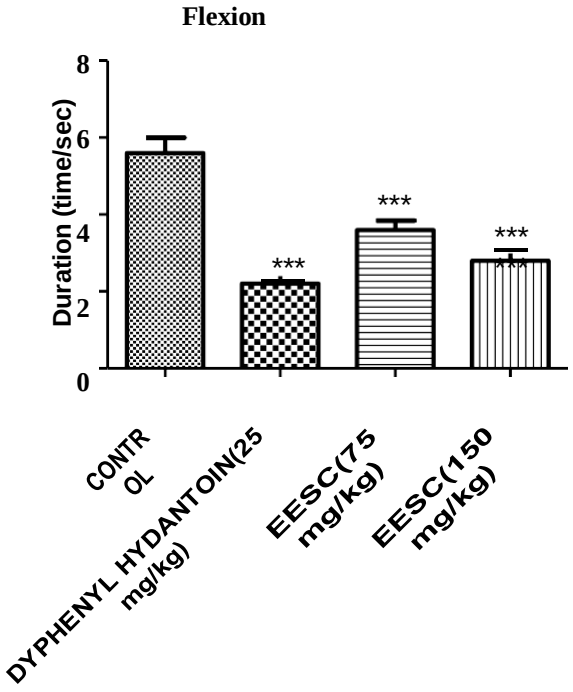


Figure No 3: Effect of EESC on duration of extension after MES

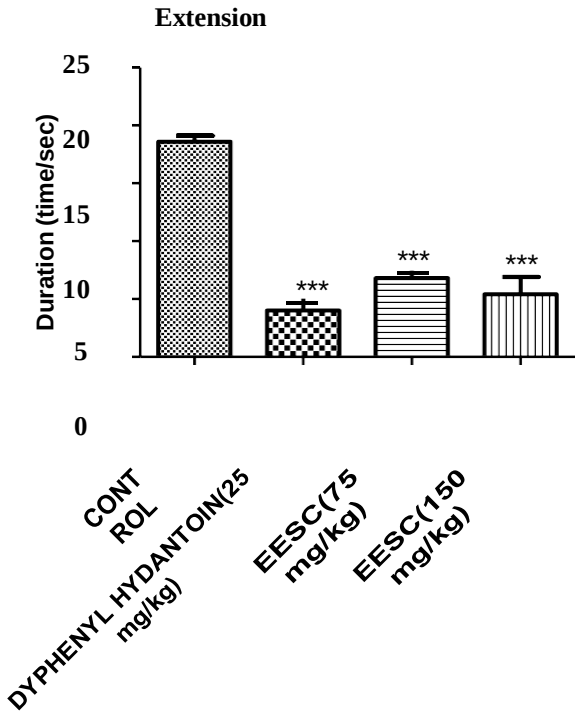
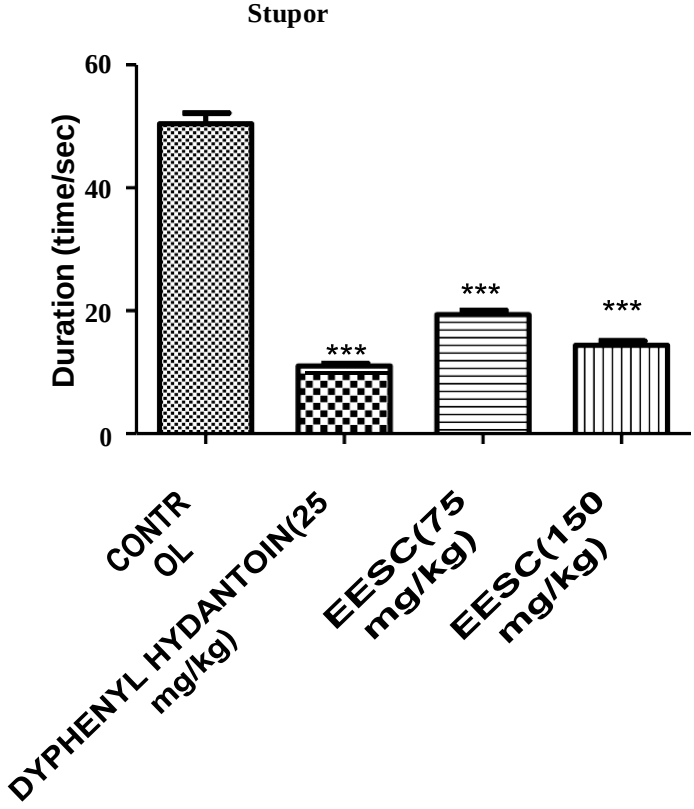


Figure No 4: Effect of EESC on duration of stupor after MES



Statistical comparison: One way ANOVA, followed by Dunett's multiple comparison test. Standard, EESC (low dose) and EESC (HIGH DOSE) are compared with control ($p<0.05$-* , $p<0.001^{**}$, $p<0.0001^{***}$)

Table No 5: Effect of Ethanol extract of *Syzygium cumini* on PTZ induced seizures models

Groups	Onset of convulsion (sec)	Duration of convulsion (sec)	Recover/ Mortality
Control	107.40 ±1.32	74.00 ±1.41	Mortality
Sodium valproate(150mg/kg)	680.60 ±1.28***	11.20 ±0.37***	Recovery
EESC (75 mg/kg)	384.40 ±2.29***	27.40 ±0.67***	Mortatility
EESC (150 mg/kg)	478.80 ±1.35***	45.80 ±0.73***	Recovery

Statistical comparison: One way ANOVA, followed by Dunett's multiple comparison test. Standard, EESC (low dose) and EESC (HIGH DOSE) are compared with control ($p<0.05$-*, $p<0.001$**, $p<0.0001$***)

Figure No 5: Effect of Ethanol extract of *Syzygium cumini on* onset ofconvulsion in PTZ induced seizure models

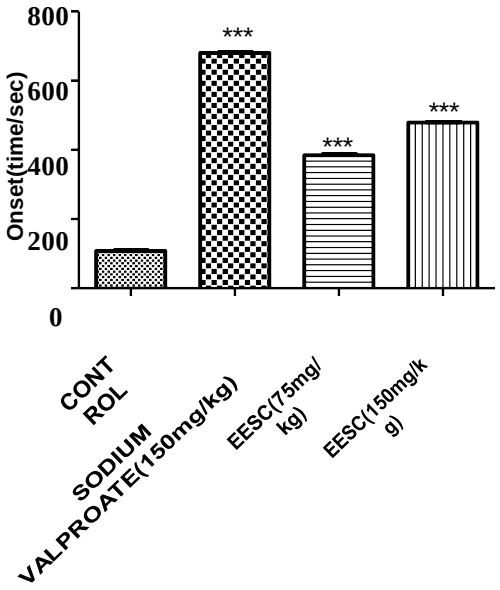
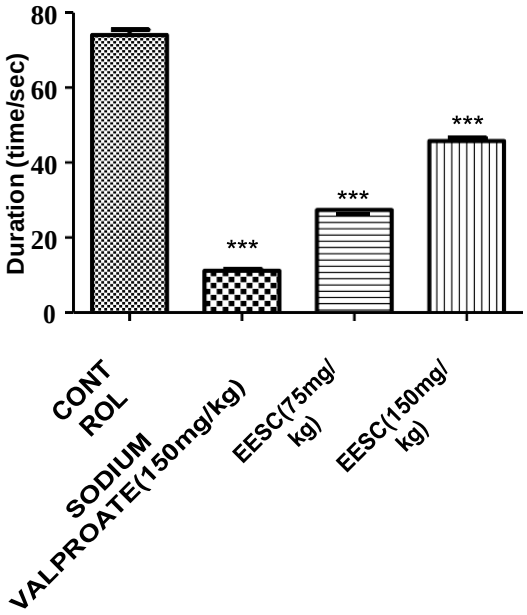


Figure No 6: Effect of Ethanol extract of *Syzygium cumini on* duration ofconvulsion in PTZ induced seizure models



***INVIVO* ANTIOXIDANT ACTIVITY**

Table No 6: Effect of EESC on brain antioxidant GSH, Total protein, LPO in MES induced seizure models

Groups	Total protein(mg/dl)	GSH(mM/mg of tissue extract)	LPO (nMoles of MDA released/ mg protein)
Control	61.8± 0.80	35.2± 0.37	57.8± 0.42
Diphenylhydantoin (25mg/kg)	13.4 ±0.40***	92.8± 0.33***	14.2 ±0.37***
EESC (75 mg/kg)	32.80 ±0.86***	73.8± 0.37***	28.8± 0.33***
EESC (150 mg/kg)	24.0± 0.44***	80.2± 0.80***	23.8± 0.40***

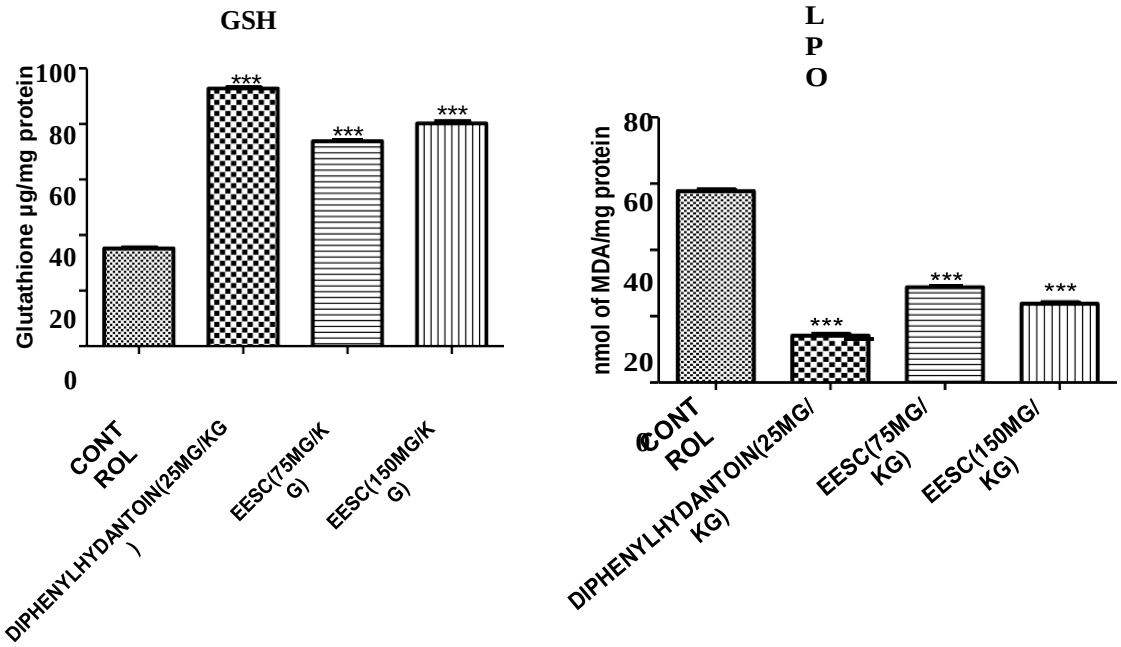
Statistical comparison: One way ANOVA, followed by Dunett's multiple comparison test. Standard, EESC (low dose) and EESC (high dose) are compared with control ($p<0.05$-*, $p<0.001$**, $p<0.0001$***)

Table No 7: Effect of EESC on brain antioxidant GSH, Total protein, LPO in PTZ induced seizure model

Groups	Total protein(mg/dl)	GSH (mM/ mg of tissue protein)	LPO (nMoles of MDA released/ mg protein)
Control	21.8± 0.33	98.0± 0.40	96.6± 0.40
Sodium Valproate (150 mg/kg)	99.2± 0.37***	42.4± 0.24***	58.8± 0.58***
EESC (75 mg/kg)	76.0± 0.44***	57.0± 0.31***	53.8± 0.37***
EESC (150 mg/kg)	86.2± 0.37***	52.0± 0.54***	55.0± 0.31***

Statistical comparison: One way ANOVA, followed by Dunett's multiple comparison test. Standard, EESC (low dose) and EESC (HIGH DOSE) are compared with control ($p<0.05$-* , $p<0.001^{**}$, $p<0.0001^{***}$

Figure No 7: Effect of EESC on brain antioxidant GSH, Total protein, LPO in MESinduced seizure models



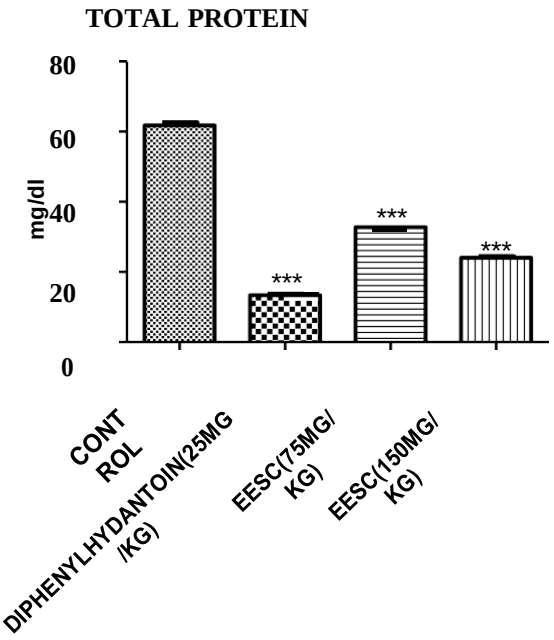
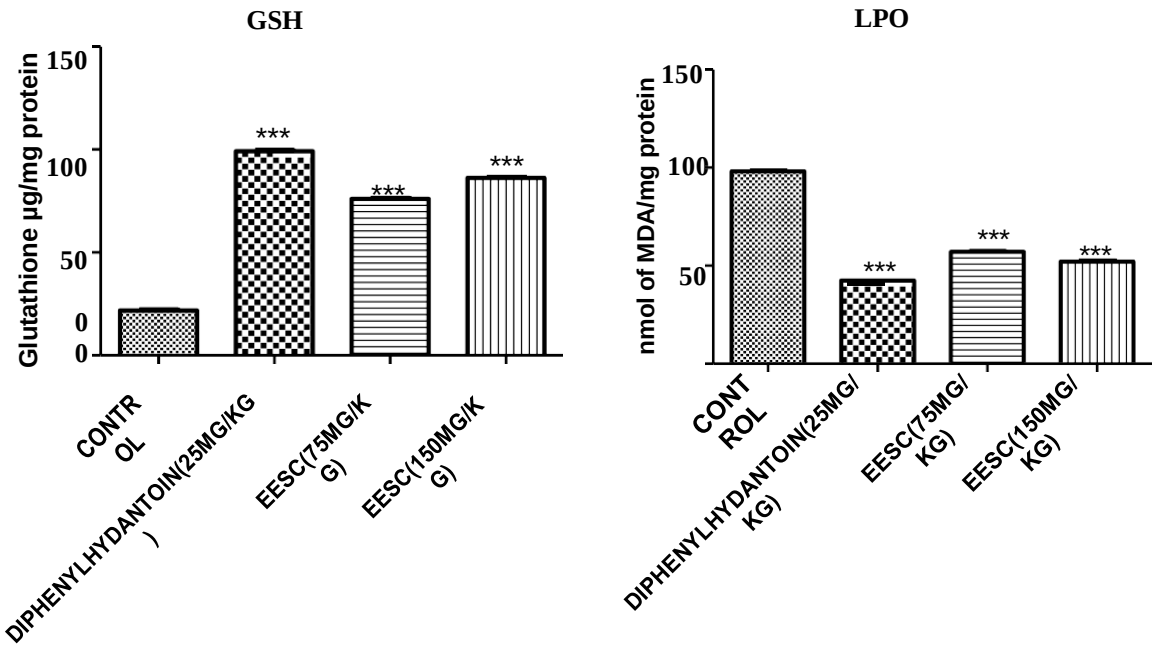
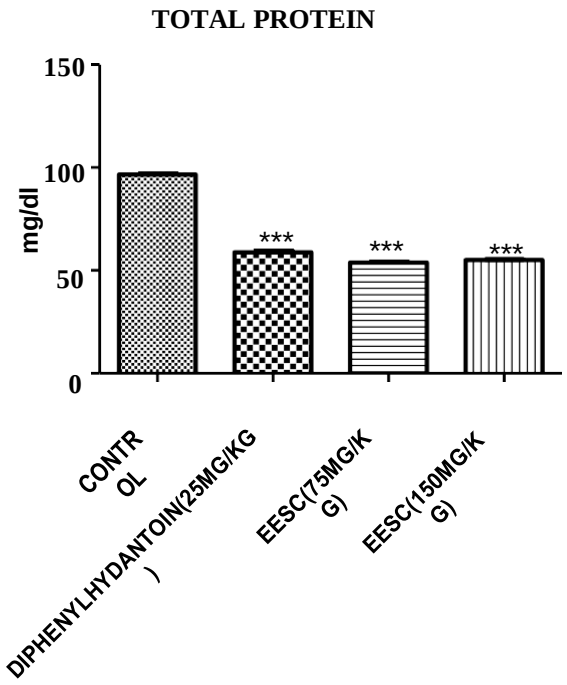


Figure No 8: Effect of EESC on brain antioxidant GSH, Total protein, LPO in PTZinduced seizure model





EFFECT OF EESC ON BRAIN NEUROTRANSMITTERS

Table No 8: Effect of EESC on neurotransmitters levels in rat brain after MES induced epilepsy

Groups	Nor adrenaline (µg/g tissue)	Dopamine (µg/g tissue)	Serotonin (µg/g tissue)	GABA (µg/g tissue)
Control	431.60±1.86	444.00±2.21	73.60±1.72	218.00±3.04
Diphenylhydantoin (25mg/kg)	584.20±1.35***	741.20±2.55***	136.80±1.65***	292.80±2.22***
EESC(75mg/kg)	530.80±2.08***	575.40±2.27***	95.80±1.28***	251.60±2.33***
EESC(150mg/kg)	545.60±2.58***	645.60±2.06***	114.60±1.77***	271.20±1.88***

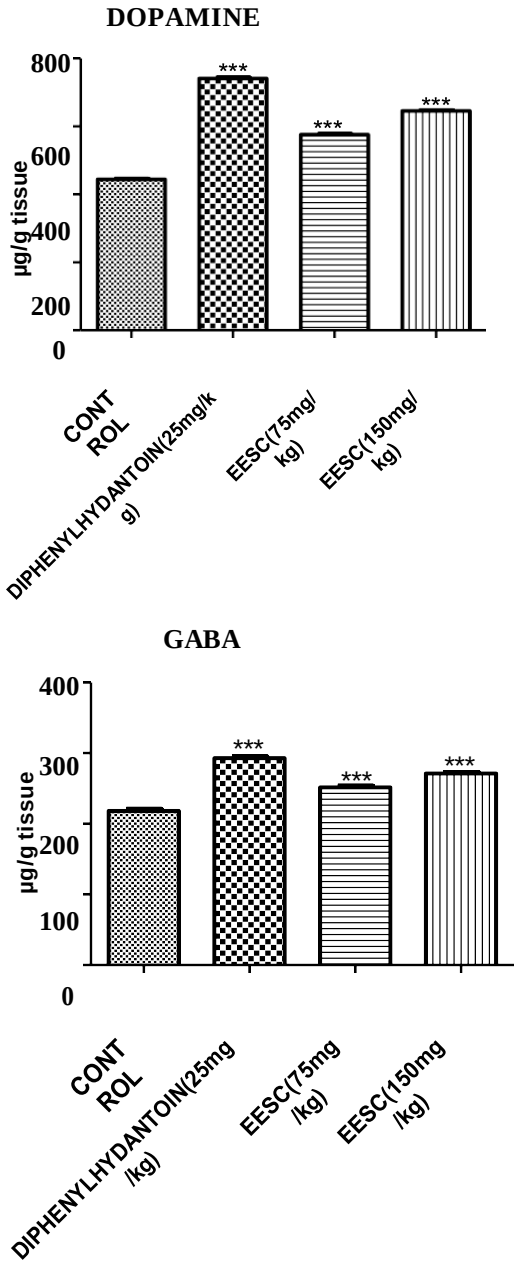
Statistical comparison: One way ANOVA, followed by Dunett's multiple comparison test. Standard, EESC (low dose) and EESC (HIGH DOSE) are compared with control ($p<0.05$-*, $p<0.001^{**}$, $p<0.0001^{***}$)

Table No 9: Effect of EESC on neurotransmitters level in rat brain after PTZinduced epilepsy

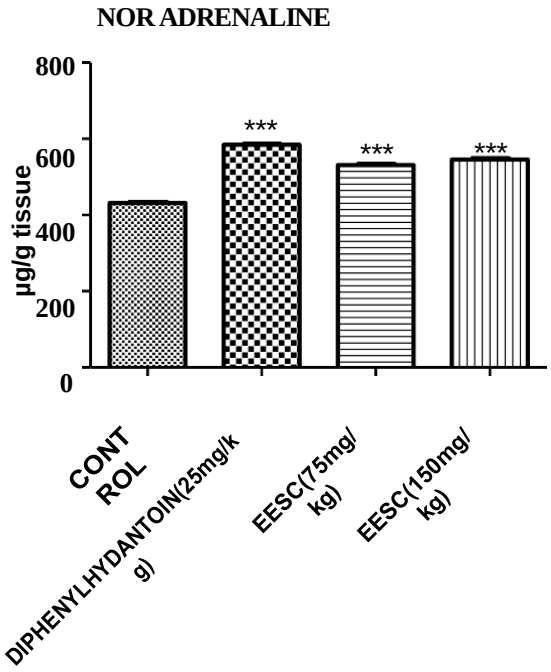
Groups	Nor adrenaline (µg/g tissue)	Dopamine (µg/g tissue)	Serotonin (µg/g tissue)	GABA (µg/g tissue)
Control	524.00±1.51	212.80±2.08	93.00±1.78	205.40±1.07
Diphenylhydantoin (25mg/kg)	790.40±1.63***	292.20±1.85***	134.80±1.98***	293.20±1.82***
EESC(75mg/kg)	682.80±1.93***	252.80±2.51***	112.20±1.98***	254.00±1.41***
EESC(150mg/kg)	749.40±1.56***	273.20±1.71***	123.20±1.01***	273.20±1.85***

Statistical comparison: One way ANOVA, followed by Dunett's multiple comparison test. Standard, EESC (low dose) and EESC (HIGH DOSE) are compared with control ($p<0.05$-*, $p<0.001$**, $p<0.0001$***)

Figure No 9: Effect of EESC on neurotransmitters levels in rat brain after MESinduced epilepsy



Effect of EESC on neurotransmitters levels in rat brain after MES inducedepilepsy



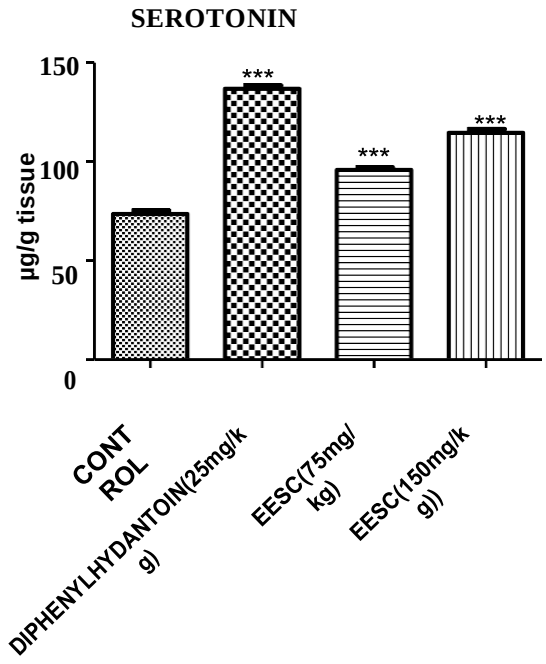
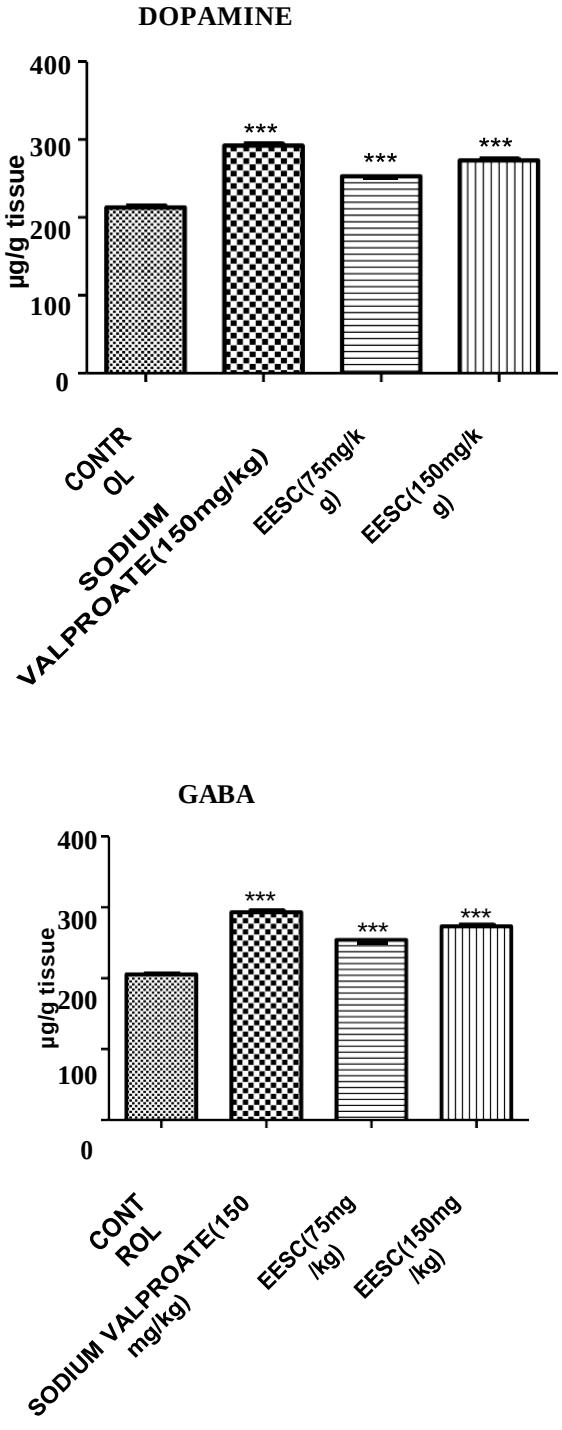
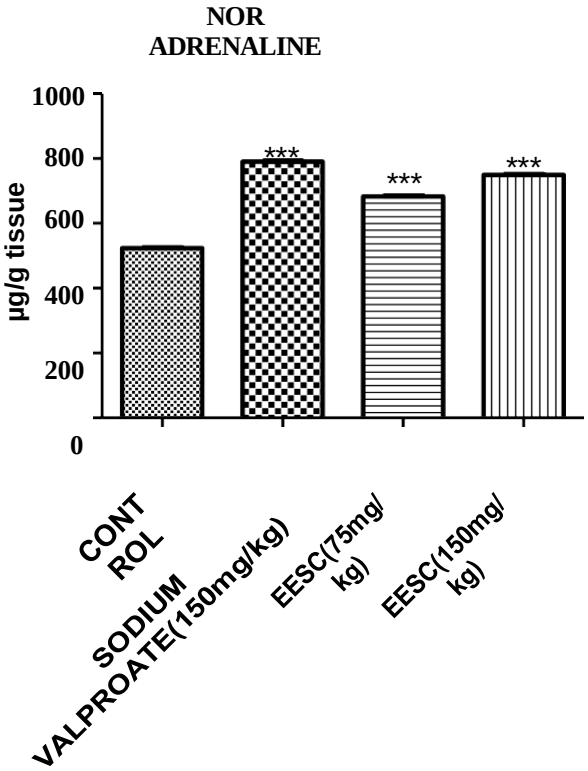
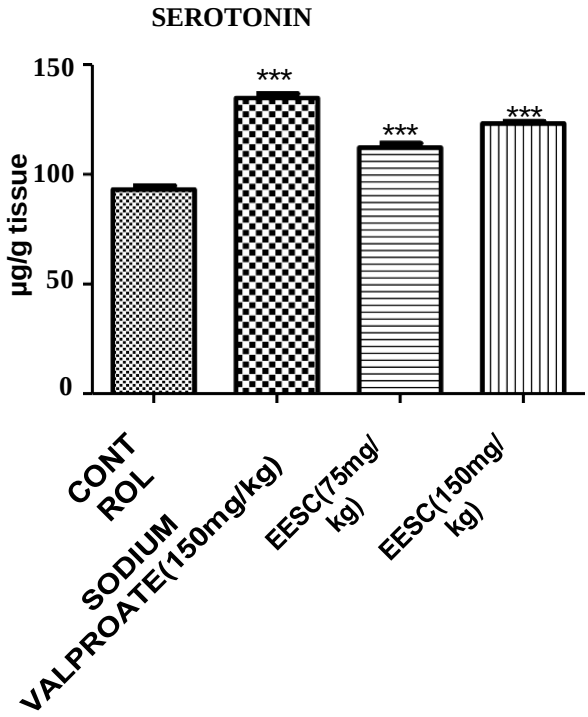


Figure No 10: Effect of EESC on neurotransmitters level in rat brain after PTZinduced epilepsy



Effect of EESC on neurotransmitters level in rat brain after PTZ induced epilepsy

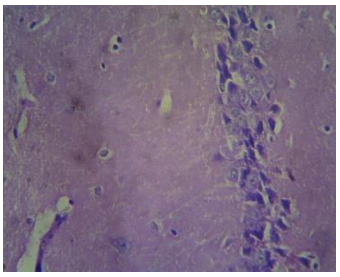




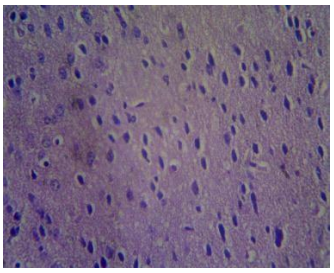
Histopathological evaluation

Histopathological evaluation of MES model

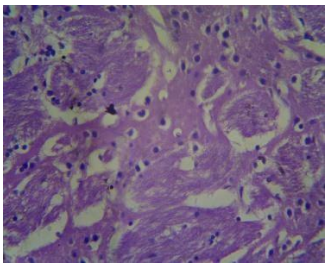
Figure No 11: Group 1: ONLY MES TREATED GROUP



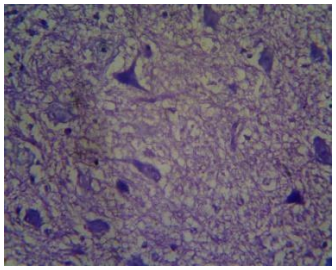
Normal hippocampus



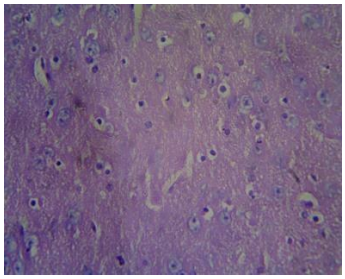
Normal thalamus



Normal corpus striatum



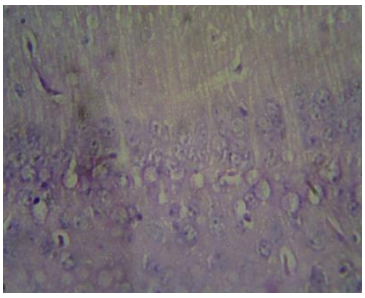
Normal substantia nigra



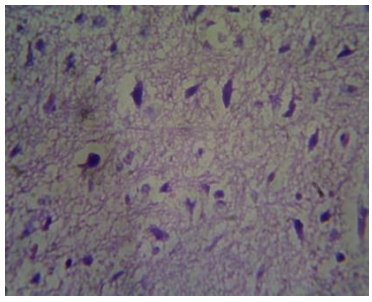
cerebral cortex with neuronal loss

From the results the rat brain shows normal hippocampus (dentate gyrus), thalamus, corpus striatum and Syzygium cumini and globus pallidus. Cerebral cortex shows neuronalloss.

Figure No 12: Group 2: MES + Standard PHENYTOIN TREATED GROUP



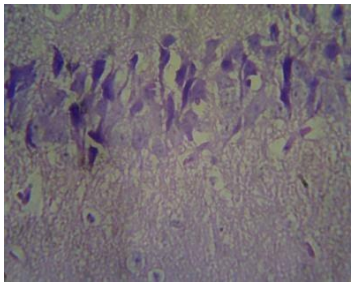
Degenerated hippocampus

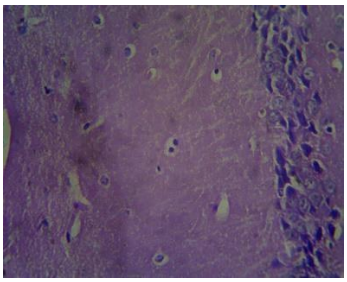


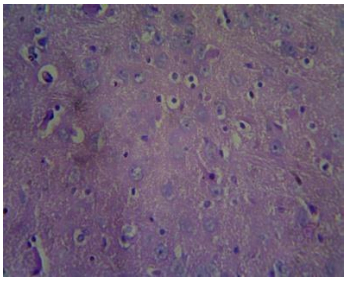
Syzygium cumini with edema

From the result rat brain shows hippocampus with degeneration, Syzygium cumini showswith edema.

Figure No 13: Group 3: MES + EESC (75 mg/kg) TREATED GROUPS

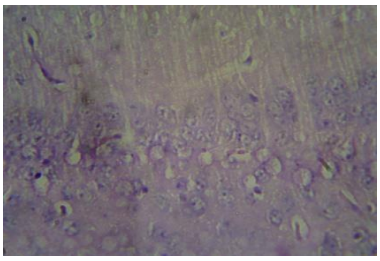

Hippocampus degeneration

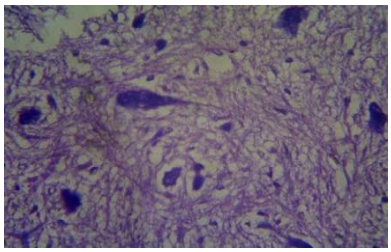

Hippocampus sclerosis


cerebral cortex with edema

From the results the rat brain shows hippocampus showing sclerosis and degeneration,cerebral cortex with edema.

Figure No 14: Group 4: MES + EESC (150 mg/kg) TREATED GROUP

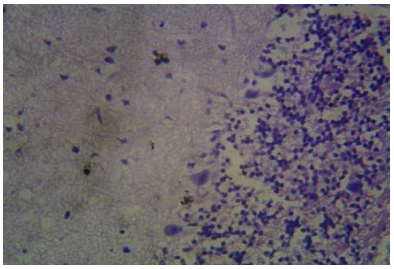

Hippocampus degeneration

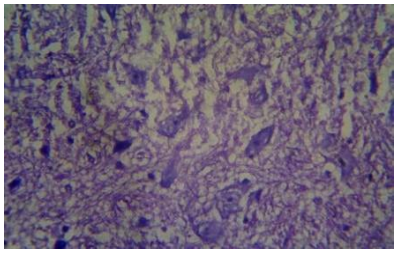

Syzygium cumini with edema

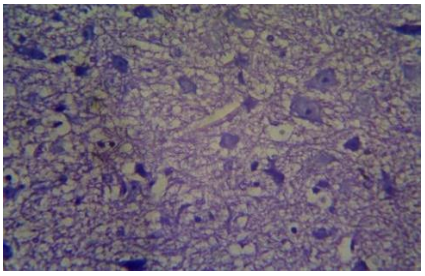
From the result rat brain shows hippocampus showing degeneration. Substantia nigra,shows neuronal loss with sclerosis.

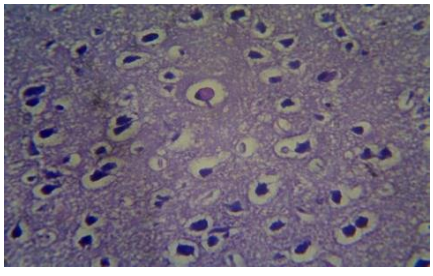
Histopathological evaluation of PTZ model

Figure No 15: Group 1: ONLY PTZ TREATED GROUP


Normal cerebellum

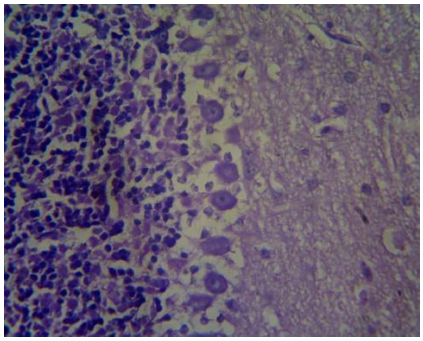

Cerebrum shows neuronal lossmolecular purkinji cell layer

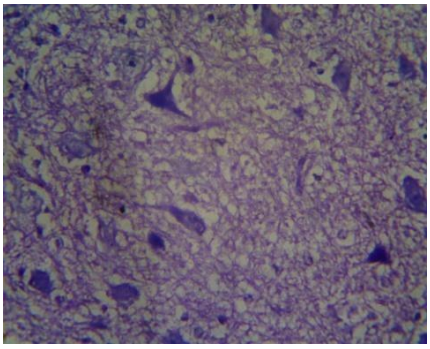

Cerebral cortex shows edema


Cerebral cortex shows piknosis

From the result rat brain shows normal cerebellum with molecular purkinji layer. Thecerebrum shows neuronal loss. Cerebral cortex shows edema and piknosis.

Figure No 16: Group 2: PTZ + SODIUM VALPROATE TREATED GROUP

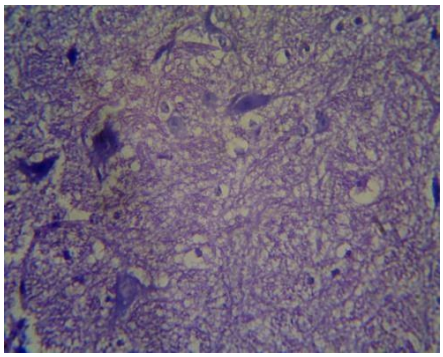


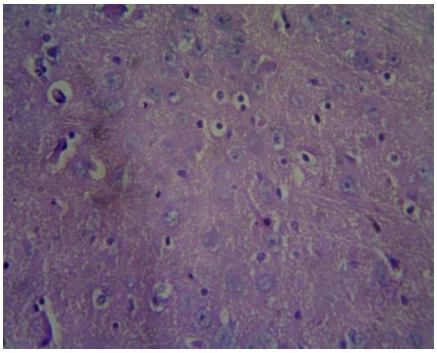


Cerebellum shows normal purkinji **Syzygium cumini**

From the result rat brain shows normal cerebellum shows normal purkinjiec cells with molecular layer and white matter. The Syzygium cumini shows neuronal loss and edema.

Figure No 17: Group 3: PTZ + EESC (75 mg/kg) TREATED GROUP

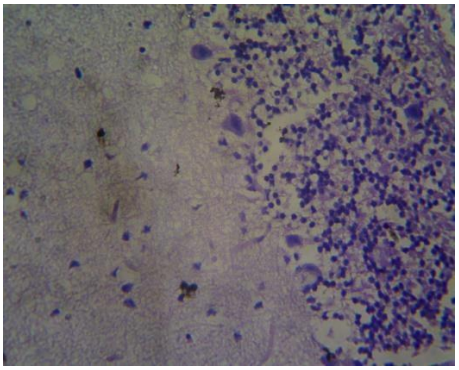


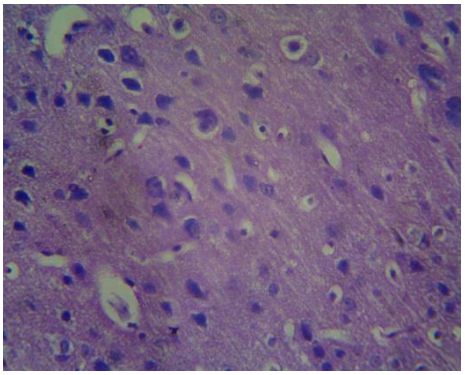


Cerebellum with normal purkinji cells **Normal cerebral cortexand molecular layer**

From the result rat brain shows cerebellum with normal purkinjiec cells and molecularlayer and white matter shows atrophy and gliosis. The cerebral cortex shows normal.

Figure No 18: PTZ + EESC (150 mg/kg) TREATED GROUPS





Normal cerebellum shows purkinji cells **Cerebral cortex shows scelorosiswith molecular layer**

From the result rat brain shows normal cerebellum shows purkinji cells with molecularlayer and white matter shows sclerosis and gliosis. The cerebral cortex shows sclerosis.

DISCUSSION:

Epilepsy is a chronic disorder of the brain that affect people worldwide. Nearly about 50-80% of the patients with epilepsy are controlled with currently available antiepileptic drugs. But these drugs cannot able to control seizures effectively in about 10-20% of the patients. The treatment of epilepsy still remains inadequate even though new anticonvulsants are being developed. Furthermore, the current therapy of epilepsy with modern antiepileptic drugs is associated with side effects, dose related and chronic toxicity as well as teratogenic effects.

Traditional systems of medicines are popular in developing countries and upto 80% of the population relies on traditional medicines/ folk remedies for their primary health care need. Hence, there is a need to discover an alternative agent from natural sources.

Syzygium cumini used as a herbal medicine and is well known for its traditional uses such as expectorants, diuretics, laxative etc. Various studies shows that the active principle diterpene alkaloids having a crucial role in treatment of epilepsy. *Syzygium cumini is* rich in diterpene alkaloids.[60] Since *Syzygium cumini have* not been studied for its antiepileptic activity, the present study was aimed to evaluate the antiepileptic activity of Ethanol extract of *Syzygium cumini*

The maximal electroshock induced convulsion in animals represents grand mal type of epilepsy. The tonic extensor phase is selectively abolished by the drugs effective in generalized tonic clonic seizure.[19] The result of the present study shows that the Ethanol extract of *Syzygium cumini at* doses 75 and 150 mg/kg significantly delayed the onset of HTLE and reduced the duration of HTLE. And also both doses completely abolished the phase of convulsion in MES induced convulsion models.

In case of PTZ induced convulsion, the result of the present study shows that the Ethanol extract of *Syzygium cumini* , at doses 75 and 150 mg/kg significantly reduced the duration and also delayed the onset of convulsion when compared to control group. PTZ may be exerting convulsant effect by inhibiting the activity of GABA at $GABA_A$ receptors. The results revealed that the EESC possess anticonvulsant activity.

Oxidative stress was described as an imbalance between generation and elimination of reactive oxygen species and reactive nitrogen species. The brain is particularly susceptible to oxidative stress because it utilizes the highest amount of oxygen than other body organs. It has been postulated that lipid peroxidation may be casually associated with certain types of epilepsy. A decrease in free radical scavenging activity may lead to an increased risk of seizure recurrence. The effect of EESC on oxidative stress in MES and PTZ induced convulsion was evaluated. EESC at doses 75 and 150 mg/kg dose showed significant decrease in LPO level.

Glutathione reductase is an important free radical scavenging compound that prevents membrane lipid peroxidation. The decreased level of reduced glutathione in control group seen in the present study indicates that there was an increased generation of free radicals and that the reduced glutathione was depleted during process of combating oxidative stress. EESC at doses 75 and 150 mg/kg dose showed significant increase in the GSH levels in brain tissue. The decrease in lipid peroxidation level and increase in the glutathione level in PTZ and MES induced convulsion models indicates that EESC exhibit good antioxidant activity.

Epilepsy may develop because of an imbalance of nerve signaling chemicals called neurotransmitters. In case of epilepsy, there may be abnormally high level of excitatory neurotransmitters(glutamate) that increase neuronal activity, while abnormally low level of inhibitory neurotransmitters (GABA) that increase neuronal activity in the brain. Hence, GABA hypoactivity and glutamate hyperactivity can enhance an epileptic seizure. In epileptic foci, GABA hypoactivity, which reduces the activity of dopaminergic neurons through a presynaptic effect through GABAA receptors. At low doses, NA can enhance an epileptic seizure, whereas at high doses, it has a protective effect on seizures. Glutamate hyperactivity is exerted through presynaptic N-methyl- D- aspartate receptors, which strongly inhibit serotoninergic neurons and through post synaptic ionotropic glutaminergic receptors, which can induce epileptic seizures. The result of the present study shows that EESC significantly increased level of inhibitory neurotransmitter GABA and also showed significant increase in the levels of DA, NA and 5-HT when compared to control group. The histopathological study shows alteration in neuronal activity in only MES and PTZ treated groups compared to standard, EESC low dose and high dose. Hence, the result indicates that EESC have good anticonvulsant activity.

CONCLUSION:

The Ethanol extract of *Syzygium cumini delayed* the onset and reduced the duration of convulsion in MES and PTZ induced convulsion models and can be used

as an adjuvant therapy against cognitive deficit in convulsions. The extract also shows significant decrease in lipid peroxidation level and increase in reduced glutathione level, indicates that EESC possess good antioxidant activity. Also, EESC significantly increased the level of inhibitory neurotransmitter GABA and also showed increase in DA, NA and 5-HT levels. Hence it can be concluded that the EESC possesses good anticonvulsant activity. Further studies are needed to explore the mechanism as well as the active principle responsible for the anticonvulsant activity of *Syzygium cumini* .

REFERENCES:

1. Ngugi AK, Bottomley C, Kleinschmidt I, Sander JW, Newton CR. Estimation of the burden of active and life-time epilepsy: a meta-analytic approach. *Epilepsia*. (2010) 51:883–90. doi: 10.1111/j.1528-1167.2009.02481.x
2. Blake RV, Wroe SJ, Breen EK, McCarthy RA. Accelerated forgetting in patients with epilepsy: evidence for an impairment in memory consolidation. *Brain*. (2000) 123:472–83. doi: 10.1093/brain/123.3.472
3. Wang Z, Lu G, Zhang Z, Zhong Y, Jiao Q, Zhang Z, et al. Altered resting state networks in epileptic patients with generalized tonic-clonic seizures. *Brain Res*. (2011) 1374:134–41. doi: 10.1016/j.brainres.2010.12.034
4. Lüders HO, Engel J, Munari C. General principles. In: Engel J, Jr., editor. *Surgical Treatment of the Epilepsies*. 2nd ed. New York, NY: Raven Press (1993). p. 137–53.
5. Lüders HO, Najm I, Nair D, Widdess-Walsh P, Bingman W. The epileptogenic zone: general principles. *Epileptic Disord*. (2006) 8:1–9.
6. Kahane P, Landré E, Minotti L, Francione S, Ryvlin P. The Bancaud and Talairach view on the epileptogenic zone: a working hypothesis. *Epileptic Disord*. (2006) 8:16–26. Stafstrom CE, Carmant L. Seizures and epilepsy: an overview for neuroscientists. *Cold Spring Harb Perspect Med*. 2015;5(6):a022426. Published 2015 Jun 1. doi:10.1101/cshperspect.a022426.
7. Morton J. *Fruits of warm climates.* Miami: Julia Morton Winterville North Carolina; p. 1987.
8. Gamble JS. *The flora of the presidency of Madras.* London: Adlard & Son LTD; 1935.
9. Hooker JD. *The flora of British India.* London: Nabu Press; 1879. p. 499.
10. Craveiro AA, Andrade CHS, Matos FJA, Alencer JW, Machado MIL. Essential oil of *Eugenia jambolana*. *J Nat Prod.* 1983; 46:591–592.
11. Ravi K, Ramachandran B, Subramanian S. Protective effect of *Eugenia jambolana* seed kernel on tissue antioxidants in streptozotocin induced diabetic rats. *Biol Pharm Bull*. 2004;27:1212–1217.
12. Ravi K, Ramachandran B, Subramanian S. Effect of *Eugenia jambolana* seed kernel on antioxidant defense system in streptozotocin induced diabetes in rats. *Life Sci*. 2004a;75:2717–2731.
13. Bajpai M, Pande A, Tewari SK, Prakash D. Phenolic contents and antioxidant activity of some food and medicinal plants. *Int J Food Sci Nutr*. 2005; 56:287–291.
14. Council of Scientific and Industrial Research . *The wealth of India.* New Delhi: Council of Scientific and Industrial Research; 1948. 1976 pp.
15. Govindu S, Adikay S. Evaluation of antiepileptic activity of chloroform extract of Acalypha fruticosa in mice. *Pharmacognosy Res*. 2014;6(2):108-112. doi:10.4103/0974-8490.128970
16. Shimada T, Yamagata K. Pentylenetetrazole-Induced Kindling Mouse Model. J Vis Exp. 2018 Jun 12;(136):56573. doi: 10.3791/56573. PMID: 29985308; PMCID: PMC6101698.